Open Accesss

Journal of Pharmacology and Therapeutics

SARS-CoV-2 : Accumulation Of Mutations With Time Decreases The Infectivity And Virulence Of RNA Viruses

Samir Kumar Patra*

Department of Life Science, National Institute of Technology, India

Author's information:
Samir Kumar Patra*
Department of Life Science, National Institute of Technology, India

Received Date: Nov 27, 2022
Accepted Date: Dec 17, 2022
Published Date: Dec 24, 2022

Abstract

The probability of evolving increases with the rate of mutation, and the possibility of extinction increases with the rate of evolution. According to my hypothesis, pharmacologically accelerating the rate of mutations in the viral progeny genomes would aid in the eradication of the virus' virulence and/or infectivity. The history of viral diseases makes this fact abundantly clear: over time, virus progeny acquire low to moderate mutations that increase virulence, and further accumulation of mutations in the following progenies results in a decrease in infectiousness and/or a loss of replicative capacity. However, because it occurs statistically, we are aware that mutations are inherently random. Given that their own polymerase lacks proofreading capacity, +ssRNA viruses have a high mutation rate.The SARS-CoV-2 mutation statistics indicate that the virus has a high rate of mutation globally and that its enhanced proofreading capacity is not very useful. It would be beneficial to the fight against the pandemic if nucleotide analogues were used with pharmaceutical products to increase the mutation in the SARS-CoV-2 genome. COVID-19

Introduction

RNA viruses exhibit higher rates of mutation, according to our understanding of the textbook and recent research (Figure 1A) [1,2]. The rate of mutation vs genome size for the two closely related biological entities, the virus and bacterium, is shown in Figure 1B [1]. We have noticed that during previous outbreaks of diseases like the Spanish flu, SARS, MARS, etc., the infectivity (the ability to infect the host) and pathogenicity (the ability to produce new virion) of those viruses climb quickly to a peak and then gradually decline (Figure 1B). I describe this phenomena in terms of the accumulation of bad mutations as seen from the viewpoint of the relevant virus. I am not including the host side in my discussion because the premise of heard immunity, especially for those who have not received a vaccine,Remdesivir, a pro-analogue of adenosine triphosphate, appeared to have a beneficial effect with severe COVID-19 [5]. However, the use of many antiviral medications also has therapeutic results, although having harmful side effects [6].

Mutation is common during RNA virus replication:

After infection, the host ribosomal machinery translates a significant portion of the infected RNA into polyproteins, which are then processed further to produce a variety of non-structural proteins (nsps) with specific functions, such as double membrane sphere formation, genome replication, production of structural proteins, and packaging to individual virion. Because their own replication machinery, the RDRP (RNA dependent RNA polymerase), does not perform any proofreading throughout the replication phase, RNA viruses have significant mutation rates.

RNA virus replication is a mutation. prone:

RNA viruses produce progeny that differ from their parents by 1-2 mutations each, and an increase in this pace would result in their extinction [7]. They are able to develop in new hosts while surviving immunological attack to a certain extent due to their inability to maintain their original DNA. A higher mutation rate in the influenza and polioviruses results in deadly mutagenesis. Exogenous mutagens may result in enough additional mutations—many of which are harmful—to make the progeny RNA viruses less fit and ultimately extirpate from the environment. However, the selection for genetic diversity and other effects of a high mutation rate push RNA viruses to near the threshold for lethal mutagenesis. Earlier analyses on RNA virus mutation rates suggested that host cell metabolic environment normal to the virus put it just under the threshold for lethal mutagenesis.

Discussion and Conclusion:

These results imply that the virus is mutating and may be evolving into SARS-CoV-2. In this situation, the contribution of the modified RDRP could be used to combat COVID-19. Currently, a number of medications are being used to treat SARS-CoV-2, including remdesivir, which works against RDRP, and lopinavir-ritonavir, which works against the primary protease enzyme [5,6].

Some of the medications have a predicted binding moiety in a hydrophobic cleft in the SARS-CoV-2 RDRP that is close to the 14408 mutation [9] [15]. Characterizing the SARS-CoV-2 RDRP functional mutation is crucial for understanding potential drug-resistant variants as well [16]. Given this and the ideas that "higher the mutation rate, higher the possibility of evolution," and "higher the possibility of evolution, higher the probability of evolution," is the likelihood of extinction" according to evolutionary theory [14], and in this case, the absence of vaccine manufacturing as well as the precise function nucleotide analogues may play in inducing higher and higher mutation, may be utilised to fight the disease. COVID-19. Along with remdesivir, the nucleotide/nucleoside analogues, such as azacitidine, may be particularly helpful [13,15].

Accelerating the mutation rate can hasten the virus' extinction, although low to medium quantities of mutations are damaging [1,11–13] since they wouldn't sufficiently impair the essential machinery, such as primary protease, the RDRP, or structural proteins such spike RBD. For such a terrible pathogen, we are unable to fix mutation at the desired area or spots [1,7], but we can increase the likelihood by increasing the mutation rate [16–18]. If a vaccination becomes available for protection in the near future, it can be claimed that virulence-prone mutations would be strengthened by antivirals and would render the vaccine ineffective sooner as well. As a result, it is highly encouraging that the SARS-CoV-2 can be combated by increasing mutation rates using nucleotide/nucleoside analogues, as has been shown for other RNA viruses [19].

Furthermore, it is encouraging that SARS-CoV-2 may have an increased mutation rate due to its ineffective proofreading accessory and large copy number similar to other RNA viruses [20]. This contribution discussed the use of nucleotide/nucleoside analogues in combination antiviral therapy for COVID-19. After SARS-CoV went extinct, SARS-CoV-2 appeared; CarrascoHernandez et al. [21] recently hypothesised that another version may develop.

References:

1. Sanjuán R, Nebot MR, Chirico N, Mansky LM, Belshaw R. Viral mutation rates. J Virol. 2010;84(19):9733-48.

2. Drake JW. Rates of spontaneous mutation among RNA viruses. Proc Natl AcadSci U S A. 1993;90(9): 4171-5.

3. Forster P, Forster L, Renfrew C, Forster M. Phylogenetic network analysis of SARSCoV-2 genomes. Proc Natl AcadSci USA. 2020;117(17):9241-3.

4. Kim D, Lee JY, Yang JS, Kim JW, Kim VN, Chang H. The architecture of SARS-CoV-2 Transcriptome. Cell. 2020;181(4):914-21.e10.

5. Grein J, Ohmagari N, Shin D, Diaz G, Asperges E, Castagna A, et al. Compassionate use of remdesivir for patients with severe Covid-19. N Engl J Med. 2020;382(24):2327-36.

6. Hung IFN, Lung KC, Tso EYK, Liu R, Chung TWH, Chu MY, et al. Triple combination of interferon beta-1b,lopinavir–ritonavir, and ribavirin in the treatment of patients admitted to hospital withCOVID-19: an open-label, randomised, phase 2 trial. The Lancet. 2020;395(10238):1695-704.

7. Peck KM, Lauring AS. Complexities of viral mutation rates. J Virol. 2018;92(14):e01031-17.

8. Pachetti M, Marini B, Benedetti F, Giudici F, Mauro E, Storici P, et al. Emerging SARSCoV-2 mutation hot spots include a novel RNA-dependent-RNA polymerase variant.
J Transl Med. 2020;18:179.

9. Biswas NK, Majumder PP. Analysis of RNA sequences of 3636 SARS-CoV-2 collected from 55 countries reveals selective sweep of one virus type. Indian J Med Res.
2020;151(5):450-8.

10. Maitra A, Sarkar, MC, Raheja H, Biswas NK, Chakraborti S, Singh AK, et al. Mutations in SARS-CoV-2 viral RNA identified in Eastern India: Possible implications for the ongoing outbreak in India and impact on viral structure and host susceptibility. JBiosci. 2020;45(1):76.

11. Shang J, Ye G, Shi K, Wan Y, Luo C, Aihara H, et al. Structural basis of receptor recognition by SARS-CoV-2. Nature. 2020;581:221-4.

12. Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, et al. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. Nature. 2020;581(7807):215-20

13. Wang Q, Zhang Y, Wu L, Niu S, Song C, Zhang Z, et al. Structural and functional basis of SARS-CoV-2 entry by using human ACE2. Cell. 2020;181(4):894-904.e9.

14. Jia Y, Shen G, Zhang Y, Huang KS, Ho HY, Hor WS, et al. Analysis of the mutation dynamics of SARS-CoV-2 reveals the spread history and emergence of RBD mutant with lower ACE2 binding affinity. bioRxiv preprint. 2020.

15. Elfiky AA. Ribavirin, Remdesivir, Sofosbuvir, Galidesivir, and Tenofovir against SARS-CoV-2 RNA dependent RNA polymerase (RdRp): A molecular docking study.
Life Sci. 2020;253:117592.

16. Gordon CJ, Tchesnokov EP, Woolner E, Perry JK, Feng JY, Porter DP, et al. Remdesivir is a direct-acting antiviral that inhibits RNA-dependent RNA polymerase from severe acute respiratory syndrome coronavirus 2 with high potency. J Biol Chem. 2020;295(20):6785-97.

17. Lynch M, Ackerman MS, Gout JF, Long H, Sung W, Thomas WK, et al. Genetic drift,selection and the evolution of the mutation rate. Nat Rev Genet. 2016;17:704-14.

18. Patra SK. Outfitting COVID-19: An effective therapeutic approach. AIJR Preprints.41: Version-1.

19. Jordan PC, Stevens SK, Deval J. Nucleosides for the treatment of respiratory RNA virus infections. Antivir Chem Chemother. 2018;26:2040206618764483.

20. Chinchar VG. Replication of viruses. Encyclopedia of Virology. 1999:1471-8.

21. Carrasco-Hernandez R, Jácome R, López Vidal Y, Ponce de León S. Are RNA viruses candidate agents for the next global pandemic? A review. ILARJ. 2017;58(3):343-58.